

CLAIMS

The current claim set of the application is presented below. Indications as to the status of the claims ("original", "currently amended", "cancelled", "new", etc.) appear in parentheses after the claim number. Deletions are identified in bold with double brackets and strikethrough (e.g. ~~[[deletion]]~~) and new text is identified in bold with underlining (e.g. new language).

1. [Currently Amended] A method for inhibiting release of a proinflammatory mediator from a mammalian cell, the method comprising:

identifying a mammalian subject suffering from, or at risk for, a disease or disorder mediated by a proinflammatory mediator; and

stimulating a sympathetic neuron of the subject in an amount effective to inhibit the release of the proinflammatory mediator;

wherein the disease or disorder mediated by a proinflammatory mediator is selected from the group consisting of allergy, anaphylactic shock, immune complex disease, organ ischemia, reperfusion injury, organ necrosis, hay fever, sepsis, septicemia, endotoxic shock, cachexia, hyperpyrexia, eosinophilic granuloma, granulomatosis, sarcoidosis, septic abortion, epididymitis, vaginitis, prostatitis, urethritis, bronchitis, emphysema, rhinitis, cystic fibrosis, pneumonitis, pelvic inflammatory disease, alveolitis, bronchiolitis, pharyngitis, pleurisy, sinusitis, influenza, respiratory syncytial virus infection, herpes infection, HIV infection, disseminated bacteremia, Dengue fever, candidiasis, malaria, filariasis, amebiasis, hydatid cysts, burns, dermatitis, dermatomyositis, urticaria, warts, wheals, vasculitis, rheumatoid arthritis, Alzheimer's disease, meningitis, encephalitis, multiple sclerosis, cerebral infarction, cerebral embolism, Guillane-Barre syndrome, neuritis, neuralgia, spinal cord injury, paralysis, uveitis, arthritides, arthralgias, osteomyelitis, fasciitis, Paget's disease, gout, periodontal disease, rheumatoid arthritis, synovitis, Sjogren's syndrome, myasthenia gravis, thyroiditis, systemic lupus erythematosus, lupus erythematosus, Addison's disease, pernicious anemia, Goodpasture's syndrome, Behcet's syndrome, allograft

rejection, graft-versus-host disease, Type I diabetes, ankylosing spondylitis, Berger's disease, Type I diabetes, ankylosing spondylitis, spinal cord injury, Retter's syndrome, Graves disease, and Hodgkins disease.

2. [Original] The method of claim 1, wherein the stimulating comprises applying an electrical pulse to the neuron.
3. [Original] The method of claim 2, wherein the electrical pulse is applied by a pulse generator.
4. [Original] The method of claim 3, wherein the pulse generator is an implantable pulse generator.
5. [Original] The method of claim 2, wherein a plurality of electrical pulses is applied to the neuron.
6. [Previously Presented] The method of claim 1, wherein the sympathetic neuron is one of the splenic nerve.
7. [Original] The method of claim 6, wherein stimulating the splenic nerve comprises applying a stimulation signal to the splenic nerve.
8. [Previously Presented] The method of claim 6, wherein the stimulation signal is applied to a splenic neurovascular bundle, a periaarterial splenic nerve, a substantially fully dissected splenic nerve or nerve bundles, splenic peritoneum, splenic tissue, celiac plexus surrounding the celiac artery, celiac ganglia, aorticorenal ganglia, greater thoracic splanchnic nerves, lesser thoracic splanchnic nerves, least thoracic splanchnic nerves, lower thoracic sympathetic trunk ganglia, upper lumbar sympathetic trunk ganglia, preganglionic sympathetic fibers, preganglionic sympathetic fibers of T8-L2, sympathetic trunk ganglia of T8-L2, white ramus communicans of T8-L2, gray ramus communicans of T8-L2, spinal ganglia of T8-L2, ventral root of T8-L2, preganglionic sympathetic

fibers of T9, sympathetic trunk ganglion of T9, white ramus communicans of T9, gray ramus communicans of T9, spinal ganglion of T9, ventral root of T9, or a combination thereof.

9. [Original] The method of claim 8, wherein the stimulation signal comprises an electrical pulse.
10. [Original] The method of claim 7, wherein the stimulation signal comprises an electrical pulse.
11. [Original] The method of claim 10, wherein the electrical pulse is applied by a pulse generator.
12. [Original] The method of claim 11, wherein the pulse generator is an implantable pulse generator.
13. [Original] The method of claim 11, wherein a plurality of electrical pulses is applied to the neuron.
14. [Original] The method of claim 1, wherein the proinflammatory mediator is a pro-inflammatory cytokine.
15. [Original] The method of claim 14, wherein the cytokine is selected from the group consisting of tumor necrosis factor alpha (TNF α); interleukin (IL)-1 α ; IL-1 β ; IL-2; IL-5; IL-6; IL-8; IL-15; IL-18; interferon (IFN- γ); platelet-activating factor (PAF); Thromboxane; soluble adhesion molecules; vasoactive neuropeptides; phospholipase A2; Plasminogen activator inhibitor (PAI-1); Free radical generation; Neopterin; CD14; prostacyclin; Neutrophil elastase; Protein kinase; Monocyte chemoattractant proteins 1 and 2 (MCP-1, MCP-2); macrophage migration inhibitory factor (MIF); and high mobility group box protein 1 (HMGB-1).

16. [Original] The method of claim 14, wherein the proinflammatory cytokine is selected from the group consisting of TNF- α ; HMGB-1; IL-1; and IL-6.
17. [Original] The method of claim 14, wherein the proinflammatory cytokine is TNF- α .
18. [Original] The method of claim 1, wherein the pro-inflammatory mediator is a chemokine.
19. Cancelled
20. Cancelled
21. [Currently Amended] The method of claim ~~[[20]]~~ 1, wherein the disease or disorder is selected from the group consisting of endotoxic shock, ~~[[appendicitis, peptic, gastric and duodenal ulcers, peritonitis, pancreatitis, inflammatory bowel disease, acute ulcerative colitis, chronic ulcerative colitis, ischemic colitis, hepatitis, nosocomial infection, Crohn's disease, diabetes, asthma,]]~~ allergy, anaphylactic shock, ~~[[arteriosclerosis,]]~~ organ ischemia, reperfusion injury, organ necrosis, sepsis, septicemia, cachexia, septic abortion, disseminated bacteremia, burns, rheumatoid arthritis, Alzheimer's disease, ~~[[coeliac disease, congestive heart failure, adult respiratory distress syndrome, cardiovascular disease,]]~~ multiple sclerosis, ~~[[diabetes,]]~~ spinal cord injury, allograft rejection and graft-versus-host disease.
22. [Currently Amended] The method of claim ~~[[20]]~~ 1, wherein the disease or disorder is endotoxic shock.
23. [Original] The method of claim 1, wherein a ganglion is stimulated.
24. [Original] The method of claim 1, wherein a postganglionic neuron is stimulated.

25. [Original] The method of claim 1, wherein a peripheral tissue or organ served by the splenic nerve is stimulated directly.
26. [Previously Presented] The method of claim 1, further comprising stimulating a vagus nerve.
27. [Currently Amended] A method of inhibiting an inflammatory cytokine cascade in a patient, comprising:
stimulating a sympathetic neuron in the patient in an amount sufficient to inhibit the inflammatory cytokine cascade,
wherein the patient is diagnosed as suffering from, or at risk for, a disease or disorder mediated by the inflammatory cytokine cascade,
wherein the disease or disorder mediated by a proinflammatory mediator is selected from the group consisting of allergy, anaphylactic shock, immune complex disease, organ ischemia, reperfusion injury, organ necrosis, hay fever, sepsis, septicemia, endotoxic shock, cachexia, hyperpyrexia, eosinophilic granuloma, granulomatosis, sarcoidosis, septic abortion, epididymitis, vaginitis, prostatitis, urethritis, bronchitis, emphysema, rhinitis, cystic fibrosis, pneumonitis, pelvic inflammatory disease, alveolitis, bronchiolitis, pharyngitis, pleurisy, sinusitis, influenza, respiratory syncytial virus infection, herpes infection, HIV infection, disseminated bacteremia, Dengue fever, candidiasis, malaria, filariasis, amebiasis, hydatid cysts, burns, dermatitis, dermatomyositis, urticaria, warts, wheals, vasculitis, rheumatoid arthritis, Alzheimer's disease, meningitis, encephalitis, multiple sclerosis, cerebral infarction, cerebral embolism, Guillane-Barre syndrome, neuritis, neuralgia, spinal cord injury, paralysis, uveitis, arthritides, arthralgias,

osteomyelitis, fasciitis, Paget's disease, gout, periodontal disease, rheumatoid arthritis, synovitis, Sjogren's syndrome, myasthenia gravis, thyroiditis, systemic lupus erythematosus, lupus erythematosus, Addison's disease, pernicious anemia, Goodpasture's syndrome, Behcets's syndrome, allograft rejection, graft-versus-host disease, Type I diabetes, ankylosing spondylitis, Berger's disease, Type I diabetes, ankylosing spondylitis, spinal cord injury, Retier's syndrome, Graves disease, and Hodgkins disease.

28. [Original] The method of claim 27, wherein the sympathetic nerve is stimulated electrically.
29. [Original] The method of claim 27, wherein a ganglion is stimulated.
30. [Original] The method of claim 27, wherein a postganglionic neuron is stimulated.
31. [Original] The method of claim 27, wherein the splenic nerve is stimulated.
32. [Original] The method of claim 27, wherein a peripheral tissue or organ served by the splenic nerve is stimulated directly.
33. [Original] The method of claim 27, further comprising stimulating the patient's vagus nerve.
34. Cancelled
35. [Currently Amended] The method of claim 27, wherein the disease or disorder is selected from the group consisting of endotoxic shock, [~~appendicitis, peptic, gastric and duodenal ulcers, peritonitis, pancreatitis, inflammatory bowel disease, acute ulcerative colitis, chronic ulcerative colitis, ischemic colitis, hepatitis, nosocomial~~

~~infection, Crohn's disease, diabetes, asthma,~~] allergy, anaphylactic shock,
[[~~arteriosclerosis,~~]] organ ischemia, reperfusion injury, organ necrosis, sepsis,
septicemia, cachexia, septic abortion, disseminated bacteremia, burns, rheumatoid
arthritis, Alzheimer's disease, [[~~celiac disease, congestive heart failure, adult~~
~~respiratory distress syndrome, cardiovascular disease,~~]] multiple sclerosis,
[[~~diabetes,~~]] spinal cord injury, allograft rejection and graft-versus-host disease.

36. [Original] The method of claim 34, wherein the disease or disorder is endotoxic shock.

37. Cancelled

38. Cancelled

39. Cancelled

40. Cancelled

41. Cancelled

42. Cancelled

43. [Original] The method of claim 27, wherein the disease or disorder is allergy.

44. [Original] The method of claim 27, wherein the disease or disorder is anaphylactic shock.

45. [Original] The method of claim 27, wherein the disease or disorder is organ ischemia.

46. [Original] The method of claim 27, wherein the disease or disorder is reperfusion injury.

47. Cancelled

48. [Original] The method of claim 27, wherein the disease or disorder is sepsis.

49. [Original] The method of claim 27, wherein the disease or disorder is septicemia.

- 50. [Original] The method of claim 27, wherein the disease or disorder is cachexia.
- 51. [Original] The method of claim 27, wherein the disease or disorder is septic abortion.
- 52. [Original] The method of claim 27, wherein the disease or disorder is disseminated bacteremia.
- 53. [Original] The method of claim 27, wherein the disease or disorder is burns.
- 54. Cancelled
- 55. Cancelled
- 56. Cancelled
- 57. Cancelled
- 58. [Original] The method of claim 27, wherein the disease or disorder is Rheumatoid arthritis.
- 59. [Original] The method of claim 27, wherein the disease or disorder is spinal cord injury.
- 60. Cancelled
- 61. [Original] The method of claim 27, wherein the disease or disorder is allograft rejection.
- 62. [Original] The method of claim 27, wherein the disease or disorder is graft-versus-host disease.
- 63. [Original] The method of claim 27, wherein the disease or disorder is multiple sclerosis.
- 64. Cancelled
- 65. Cancelled
- 66. Cancelled

67. Cancelled

68. [Original] The method of claim 27, wherein the disease or disorder is Alzheimer's disease.

69. Cancelled